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CERTIFICATE

This is to certify that "**QT DISPERSION IN ACUTE MYOCARDIAL INFARCTION**" is bonafide work done by **Dr. JERIN CHERIAN MATHEW** post graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10 under my guidance and supervision in fulfillment of regulations of The Tamilnadu Dr. M.G.R. Medical university for the award of M.D. Degree Branch I, Part II (General medicine) during the academic period from March 2004 to March 2007.

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CONTENTS

INTRODUCTION

Coronary artery disease is the leading cause of death worldwide. Its first and only symptom may be fatal acute myocardial infarction. Early detection offers the greatest chance of slowing or even abating the disease process before it progresses. Infact early diagnosis is critical in saving precious lives.

Prognosticative management based on various parameters of ECG have been proposed. Some of the proposed techniques include T wave alternans, heart rate variability, QTc interval and QTc dispersion. Of these QTc dispersion which is defined as the difference between the longest and the shortest QTc interval is undergoing rigorous assessment.

Over the past ten years quite a few studies have been published evaluating QTc dispersion as a predictor of arrhythmias and sudden cardiac death. Indian studies for the same are very few. Hence a study of QTc dispersion in acute myocardial infarction stratifying the population into various subgroups and type of infarct was planned. A control group was also taken to find the normality of QTc dispersion values. The study also looked into the effect of drugs, thrombolysis on QTc dispersion. Finally the study considered the effect of QTc dispersion on mortality with regard to its prognostic and preventive implication.

AIMS AND OBJECTIVES

To assess the degree of QTc dispersion in patients getting admitted to Intensive Coronary Care Unit of Government Royapettah Hospital / Kilpauk Medical College, Chennai with acute myocardial infarction at the time of admission, post thrombolysis and one day after admission.

To study and compare QTc dispersion patterns in various types of myocardial infarction.

To find out whether any association exist between variables such as age, sex, diabetes, hypertension, smoking and QTc dispersion.

To study association between QTc dispersion and cardiac arrhythmias, left ventricular failure and death during the first twenty four hours after acute myocardial infarction.

To find out the normal range of QTc dispersion in the community and compare with those with acute myocardial infarction.

Review of Literature

REVIEW OF LITERATURE

Attempts to characterize the abnormalities of ventricular repolarization from the surface electrocardiogram (ECG) have a long history. Precise mathematical approaches can be traced back to the 1960s (1). For clinical purposes, however, the ECG based assessment of ventricular repolarization has traditionally been limited to the measurement of the QTc interval and to the description of the polarity and shape of the T wave often using vague terms such as “nonspecific ST segment and T wave changes.”````

In 1990, a report by the group led by the late Professor Campbell revived an old idea of the interlead differences in the QTc interval duration. The range of the durations termed “QTc dispersion" was proposed as an index of the spatial dispersion of the ventricular recovery times (2). It was proposed that the different myocardial regions had different ECG signals and hence, QTc dispersion is an almost direct measure of the heterogeneity of myocardial repolarization. The cardiological community welcomed the idea. The methodological simplicity and the promise of solving

the old and much debated problem of regional information within the standard ECG were appealing.

Since the first publication, the cardiological literature has been flooded by articles reporting QT dispersion in practically every cardiac as well as many noncardiac syndromes and diseases. However, voices of concern about the validity of the concept and the methodology of the measurement were raised repeatedly. Today, after a decade of the "QT dispersion era," some conclusions may be drawn from the wide spectrum of opinions (3).

Pathophysiology of QTc dispersion

The initial concept of QTc dispersion seemed to be based on a sound logic. The link between the dispersion of ventricular recovery times and arrhythmias had been demonstrated repeatedly (4, 5, 6). It was also believed that the standard surface ECG contains regional information. Therefore, finding increased QTc dispersion in patient groups in whom the heterogeneity of the ventricular recovery times was previously established, it was assumed that QTc dispersion is a reflection of the dispersion of ventricular recovery times. The validity of the concept seemed to be further consolidated by studies correlating intracardiac monophasic action potentials (MAPs) with various QTc dispersion indices.

Higham et al. (7) recorded epicardial MAPs during cardiac surgery and measured directly the dispersion of recovery times as

well as surface QTc dispersion during sinus rhythm and during ventricular pacing. They found a high positive correlation between the MAPs and ECG dispersion indices. Later, using a custom-built rabbit heart setup with simultaneous recording of MAP and 12-lead ECGs, Zabel et al. (8) showed that the dispersions of the QT and JT intervals were significantly correlated with the dispersion of 90% duration of the action potential duration (APD_{90}) and with the dispersion of recovery times. The same authors also confirmed this in patients with 12-lead ECGs recorded within 24 h of the MAPs (9). These studies were generally interpreted as a proof of QTc dispersion representing regional variations in the duration of the ventricular action potentials.

Serious arguments against this concept originated from the electrocardiographic lead theory. If the majority of the information about the ventricular electrical activity is contained in the spatial QRS and T loops, the major reason for the difference between separate leads has to be the loss of information from the projection of the loop into the separate leads (10). Macfarlane et al. (11) and Lee et al. (12) showed independently that QTc dispersion can also be found in the so called derived 12-lead ECGs, i.e., ECGs reconstructed from the XYZ leads, which naturally contain no regional information.

Kors et al.(13) further contributed to the understanding of the interlead differences. They found that QTc dispersion was

significantly different between patients with narrow (54.2 ± 27.1 ms) and wide T loops (69.5 ± 33.5 ms, P <0.001). They also showed that in each of the six limb as well as the six precordial leads, the difference between the QTc interval in a given lead and the maximum QTc interval was dependent on the angle between the axis of the lead and the axis of the terminal part of the T loop.

Punske et al. (14) compared the spatial distribution of the QTc intervals from high resolution maps on human body surface. These studies showed convincingly that the interlead differences of the QTc intervals are a reflection of morphology of the T wave loop and could be quantified .

Most recently, Malik et. al. (15) proposed a new ECG processing technique to distinguish the T wave signals representing the three dimensional movement of the ECG dipole from the nondipolar components likely to be related to regional heterogeneity of myocardial repolarization.

Hence, it is reasonable to conclude that the dispersions of ventricular recovery times measured with MAPs and QTc dispersion are direct and indirect expressions of repolarization abnormalities that are likely to correlate even without any mechanistic link. General abnormalities of ventricular repolarization, not only those leading to regional dispersion of recovery times modify the spatial T wave loop. As a result of any

abnormality, projections of the loop into the individual ECG tracings become more difficult to be localized. The effect of local dispersion of repolarization on the morphology of the T wave loop explains the (indirect) link between MAP recordings and QTc dispersion. Thus, T wave loop dynamics and the variable projections of the loop into individual ECG leads seem to be the true mechanistic background of QTc dispersion.

The studies of the link between the T loop morphology and QTc dispersion also confirmed what was empirically known long ago : the more abnormal the T wave morphology in separate leads, the more difficult and unreliable the localization of the T wave offset in each lead and, consequently, the greater the likelihood of an increased QTc dispersion. As Kors et al. (13) demonstrated, variations of the T loop morphology lead to variations in the practically unmeasurable final part of the T wave, i.e., the proportion of the signal falling within the noise bang. Thus, variations of the T loop morphology may lead to both true variations in the length of the projections of the T loop onto the separate leads and to an increased measurement error.

Projections of T loops with different shapes and at different angles to the axis of the lead result in T waves with different amplitude and morphology. Only an insignificant proportion of the final part of a T wave with high amplitude may be unmeasurable because of falling into the noise band. T waves with smaller

amplitude as a result of wider T loop or elongated loop at different angle have a greater proportion of their final parts falling into the noise band. Thus, the measurable QT interval can almost coincide with the real end of repolarization or be significantly smaller (13).

QTc dispersion is a result of both difference in real duration and measurable duration of QTc intervals. Two hypothetical T waves of the same amplitude have different offset when the heart vector becomes perpendicular to the axis of one of the leads. This results in "real" dispersion of the QTc intervals. In addition, different proportion of the final part of the two T waves is below the threshold level (e.g. with an automatic threshold method). This leads to the measured dispersion of the QTc intervals, which is different from the real dispersion.

It is now clear that QTc dispersion is merely a crude and indirect measure of general repolarization abnormalities. At the same time, disproving this hypothesis is not a good reason for stating that "QTc dispersion does not exist." QTc dispersion is clearly only a very approximate and rather simplistic expression of repolarization abnormalities that suffers from a poor pathophysiologic concept as well as, from methodological difficulties. However, regardless of the crudeness of the expression, abnormalities of the repolarization are of significant importance (16, 17). Even very indirect and very approximate measure of T wave

loop abnormalities may still have some, though restricted, informative value.

Measurement of QTc dispersion

It has been known for decades that manual determination of the T wave offset is very unreliable (18). Unfortunately, available automatic methods have not proven their superiority. The main sources of error, both for human observes and computers, are low T wave amplitude (19, 20) and merges of T waves with U and / or P waves. The morphology of the T wave also strongly influences QT interval measurement.

Several basic algorithms for automatic determination of the T wave end are available. The threshold methods localize the T offset as an intercept of the T wave or of its derivative with a threshold above the isoelectric line, usually expressed as a percentage of the T wave amplitude. The slope methods determine the T offset as an intercept between the slope of the descending part of the T wave and the isoelectric line, or a threshold line above it. The slope can be the steepest tangent computed by various line fitting algorithms or a straight line through the inflex point and the peak of the T wave. Obviously, the measured values of the QT interval depend on the shape of the descending part of the T wave. The amplitude of the T wave strongly influences the reliability of both automatic (19 and 21) and manual (20) measurement.

U wave

The origin of the U wave remains disputed. The theories that attributed the U wave to the delayed repolarization of the His-Purkinje fibre (22) or to mechanoelectrical mechanism (23), were superseded by the M-cell theory by Antzelevich et al (24). However, later experiments by the same group showed that what is often interpreted as a "Pathologically augmented U wave" or "T-U complex" is in fact a prolonged biphasic T wave with an interrupted ascending or descending limb (25). Manual measurement is even less reliable for certain T-U patterns, e.g. when the T wave is flat or inverted and the U wave augumented. Repolarization pattern of complex morphology are frequently classified differently by different observes, leading to substantial variability of the measurement (26).

Probably, electrophysiological mechanisms responsible for usual "physiologic" U wave are different from those leading to abnormal gross U waves, for instance those seen in congenital and acquired long QT syndrome. All repolarization signal originating from repolarization of ventricular myocardium should belong to the T wave. In this sense, the concept of biphasic and other unusually shaped T waves is more appropriate than a distinction between the T wave and an augmented U wave which may lead to serious underestimation of QTc interval.

A pattern resembling a U wave may also originate from slow afterdepolarization of ventricular myocytes. Distinction of such a pattern from bizarre T wave may be very difficult. At the same time, in practical QTc interval measurement signs of after depolarizations indicate the same proarrhythmic danger as bizarre T wave shapes and prolonged QT interval.

Thus, in all cases that are difficult to reconcile, augmented U waves should be preferably included into the T wave. Only distinction between T wave and clearly physiologic U waves of small amplitude should be attempted when measuring QTc interval.

Already in 1952, Lepeschkin and Surawicz (27) described and classified various patterns of T and U wave merging and suggested methods for determining the end of the T wave when "buried" within the U wave. They showed that, depending on the pattern of T-U wave merging, either the intersection of the tangent to the downslope steepest point with the isoelectric line, or the nadir between the T and the U wave is closer to the "real" T wave end. The tangent method was proposed merely as "… an attempt to determine the true end of the T wave in cases of partial merging of T and U …" (27), rather than as a universal method for determining of the end of the T wave.

In a recently published extensive review, Surawicz (28) summarized the available knowledge that could help distinguish normal or abnormal U wave merging with a T wave.

JT dispersion

In experimental and clinical studies, Zabel et al. (8, 9) showed that the QTc dispersion value reflect better the dispersion of the recovery times than the action potential duration. On the other hand, the JT dispersion reflected better the dispersion of action potential duration (APD_{90}). Consequently, some authors suggested the QTc and JT dispersions to be used as separate entities rather than mutual surrogates (19, 30). However, neither the QTc dispersion nor the JT dispersion reflect directly the dispersion of the ventricular recovery time or of the action potential duration. The dispersion of various repolarization duration intervals is merely an indirect measure of general repolariztion abnormalities. It is therefore questionable whether JT dispersion offers any real complement to the QTc dispersion, except possibly in cases of conduction abnormalities such as bundle branch block.

The Q wave dispersion, although significantly smaller than the T wave offset dispersion, may also influence QTc dispersion (31, 32). Traditional manual measurement, as well as some computer algorithms, assesses the Q wave onset separately in each lead (33), whereas other computer algorithms use a common, lead-

independent Q onset (34, 35). This may account for part of the variability between different algorithms.

Measurement Features

Theoretically, an accurate assessment of QTc dispersion requires all 12 lead of the ECG to be recorded simultaneously in order to avoid the effect of QT dynamicity due to heart rate changes. Therefore, simultaneous 12 lead recordings have been proposed as a "gold standard" for QTc dispersion measurement. On the other hand, it is possible that the slow dynamicity of the QT interval (36) renders QTc dispersion measurement based on simultaneous recording of six or even only three recording during ectopic free sinus rhythm acceptable for practical purposes.

Influence of heart rate

Many studies, including large prospective evaluations (37, 38) used the so-called corrected QTc dispersion, i.e., the dispersion of the QT intervals corrected for heart rate by some formula. Although the applications of additive formulae for heart-rate correction such as those proposed by Hodgets et al. (39) and in the Framingham Study (40) render identical values for QT dispersion and QTc dispersion.

Although experimental and clinical data show that the rate, the rhythmicity and the site of impulse origin can influence the

dispersion of the ventricular recovery time (41, 42, 43), this has never been shown for QTc dispersion. Clinical (44) and experimental (45) studies failed to find correlation between heart rate and the dispersion of ventricular recovery times measured with MAPs or QT dispersion.

The exact relation between the heart rate and the dispersion of recovery times is still and unresolved issue. It is certain, however, that QTc dispersion measured in the standard 12-lead ECG does not depend on the heart rate in the same way as the QTc interval (46).

Influence of the number of ECG leads and of the ECG lead system

The number of measurable leads in the standard ECG also influences the range of QTc interval durations. Some researchers proposed a correction factor dividing QTc interval range by the square root of the number of measurable ECG leads, leading to the so called adjusted QTc dispersion (50). Hnatkova et al. (47) showed that this formula results in a reasonable correction of mean values of QTc dispersion in normal ECGs. However, they also showed that the individual errors caused by omitting separate leads are very substantial. Consequently, it is not appropriate to compare results based on QTc interval values measured in ECGs of very different number of measurable leads.

Many clinical studies have measured QTc dispersion only in the six precordial leads. In addition, other lead combinations, such as the orthogonal XYZ or "quasiothogonal" I, aVF or V2 leads, have also been studied. It was reported that although, as one would expect, QTc dispersion is decreased when a smaller number of leads used for QTc measurement. QTc dispersion differences between different patient groups can still be detected with the three leads (aVF, V1, V4) that are most likely to contribute to QTc dispersion (51) : the limb leads (52), the orthogonal (X,Y,Z) (53 and 54) or the quasiorthogonal leads aVF and V2 (51 52 and 53). Clearly, practically any lead combination may detect abnormalities in the morphology of the T loop and translate them into increased values of QTc dispersion. On the other hand, the more projections of the T loop into different leads with different axes are used, the more sensitive the measurement becomes. Unfortunately, as already mentioned, none of this directly translates into an increased regional heterogeneity of recovery times. Therefore there is little point in continuing the quest for the "perfect lead combination" for QTc dispersion measurement.

Reliability of QTc dispersion assessment

Many studies have shown inter and intraobserver variability of manually measured QTc dispersion. The errors reach the order of the differences between normal subject and cardiac patients. Relative errors of 25-40% of interobserver and intraobserver

variability of manual measurement of QTc dispersion have been reported (27 and 55), and opposed to relative errors <6% for manual measurement of the QTc interval (55). Occasionally, substantially better reproducibility of manual measurement of QTc dispersion has also been reported, with interobserver variability of 13-18% (56) and even 5% (57). Explanations of these discrepancies can only be very speculative. Because a majority consensus clearly agrees on poor reproducibility of QTc dispersion measurement a wishful bias was likely involved in some reports presenting very low measurement errors.

In addition to the differences in the investigated population, the variations of the results can be attributed to differences in the measurement method (manual measurement with caliper or rule) (58), application of a digitizing board with or without magnifications, on screen measurement with electronic calipers, the noise level, and the paper speed at which the ECGs were recorded (20). In a technical study, Malik and Bradford (59) showed that even the "gold standard" manual measurement using the digitizing board, can produce intraobserver variations corresponding to purely error-related QTc dispersion >40 ms and >60 ms in 20% and 10% of observers, respectively.

The available automatic methods for QT measurement have not shown a superior reproducibility. For example, Yi et al. (60) reported that the immediate reproducibility (in sequentially

recorded ECGs) of various QTc dispersion indices measured with a downslope tangent method in healthy volunteers varied between 16% and 44%.

Many studies tried to validate automatic algorithms against manual measurement by experienced ECG readers. The results were disappointing showing large difference (21, 62, 63 and 64). Savelieva et al. (63) investigated the agreement between automatic (downslope tangent) and manual QTc measurement in normal subjects and patients with HCM. The agreement between the two methods of QTc interval measurement was poor and lower in normal subjects than in HCM patients. The agreement between automatic and manual measurement of QTc dispersion was even much worse.

Clinical studies

A review of the extreme abundance of studies on QTc dispersion published over the past decade reveals an amazingly wide range of QTc dispersion values in both "positive" and "negative" studies, and a complete lack of any tendency towards establishing reference values. For example, large studies (67) or literature reviews (68) suggesting QTc dispersion of 65 ms as an upper normal limit in healthy subjects were published alongside reports claiming QTc dispersion >40 ms to have 88% sensitivity

and 57% specificity for prediction of inducibility of sustained ventricular tachycardia during and electrophysiology study (69).

QTc dispersion in normal subjects and in the general population

Literature reviews found the QTc dispersion to vary mostly between 30 and 60 ms in normal subject (70 and 71), although average values around 70 ms were also reported. In 51 studies (40 published during the past three years) in which QTc dispersion was measure in 56 subgroups with a total of 8,455 healthy subjects of various ages (including three large studies of healthy children (72, 73 and 74), found mean QTc dispersion values (QT maximum-QT minimum) to range from 10.5 ± 10.0 ms (75) to 71 ± 7 ms (76). The weighted mean ± SD from all these studies is 33.4 ± 20.3 ms while the median in 37 ms. Moreover, most researchers reported a wide overlap of values between normal individuals and different patient groups..

Published reports show either no statistically significant difference in QTc dispersion between the genders (11, 73) or marginally greater values in men (77, 78). Age related differences less of than 10 ms were reported and appeared to be statistically significant in some studies (79, 80) but not in others (72, 73). For example, in the study by Savelieva et al. (81) on more than 1,000 healthy subjects, QTc dispersion was 29.1 ± 17.8 ms in the age

group of 17 to 29 years and 21.7 ± 13.3 ms in the age group of 50 to 80 years (P<0.0001). However, in another large study, Macfarlane et al. (11) found no significant age differences (QTc dispersion of 23.6 ± 7.7 ms, 24.8 ± 8.2 ms, 24.8 ± 8.5 ms and 24.5 ± 9.8 ms in the age group of < 30, 30-40, 40-50 and >50 years respectively). In this study, no age differences of QTc dispersion were found in 1,784 neonates, infants and children divided in 16 age group from >24 h to <15 years of age.

Several large prospective studies published recently assessed the predictive value of QTc dispersion for cardiac and all-cause mortality in the general population. In the Rotterdam study (37) QTc dispersion was found to predict cardiac mortality in a general population of 5,812 adults of 55 years or older, followed up for 3 to 6.5 years.

In the Strong Heart Study (38) the predictive value of the "corrected" QTc dispersion was assessed in 1,839 American Indians followed up for 3.7 ± 0.9 years. Heart rate corrected QT interval assessed as a continuous variable remained a significant and independent predictor of cardiovascular mortality in both univariate and multivariate Cox Proportional Hazard models, with 34% increase of cardiovascular mortality for each 17 ms increase in QTc dispersion in multivariate analysis. In multivariate analysis QTc dispersion >58 ms (the upper 95^{th} percentile in a separate population of normal subjects) was associated with a 3.2 – fold

increased risk of cardiovascular mortality (95% confidence interval (CI) 1.8-5.7). Unfortunately, no values for the uncorrected QTc dispersion or the simple resting heart rate were provided. Thus, the possibility of the strong predictive power being maintained by the differences in heart rate cannot be excluded.

The West of Scotland Coronary Prevention Study (WOSCOPS) (82) included 6,595 middle-aged men with moderately raised cholesterol but no previous MI. In a multivariate analysis, and increment of 10 ms in QTc dispersion increased risk for death of coronary heart disease or nonfatal MI by 13% (95% CI 14% to 22%, $p = 0.0041$). QTc dispersion >44 ms carried an increased risk of 36% (95% CI 2% to 81%, $p = 0.034$) compared with QTc dispersion <44 ms. On the other hand, this cutoff level of 44 ms had a sensitivity of only 8.8% with a specificity of 93.8%. The area under the receiver operator characteristic curve was only 54%. Indicating an almost complete lack of predictive power of QTc dispersion.

QTc dispersion in cardiac disease

There is a clear tendency towards increase of QTc dispersion in various cardiac diseases, with highest mean values reported in long QT syndrome, "the pure global repolarization disease". On the other hand the overlap of values between patients with different cardiac diseases, between patients and normal subjects, and the wide variations of values within each cardiac disease render any

attempt at establishing reference values fruitless. However, patients with various clinical symptoms, with and without arrhythmias, and on various medications have been included in these pooled studies, which probably accounts for part of the variation.

Generally, QTc dispersion is increased in acute MI, although mean values form 40 ±b 18 to 162.3 ± 64.8 ms have been reported (75, 83). Although QTc dispersion is increased in the chronic phase of MI and in other chronic forms of ischemic artery disease, there seems to be a trend towards lower values compared with the acute phase of MI, possibly due to the spontaneous dynamicity or to revascularization procedures. Some authors did not find significant differences in QT dispersion between patients with chronic MI or other forms of chronic CAD and normal subject (84, 85).

Compared with healthy controls, an increased QTc dispersion has been reported in heart failure and left ventricular dysfunction of various origin (93, 94, 95, 96 and 97), in patients with arterial hypertension irrespective of the presence or absence of hypertrophy (98), in HCM patients compared with healthy controls (99, 100 and 101), in long QT syndrome (102, 103 and 104) and in many other cardiac and even noncardiac disease. However, some studies have found QTc dispersion values not significantly different between healthy subjects and patients with heart failure (105), patients

with LVH as result of physical training (106, 107 and 108), or between patients with and without LVH (109).

Many studies tried to correlate QTc dispersion with the extent or the localization of the pathological process of various diseases. Some studies have shown greater QTc dispersion in anterior compared to inferior MI (110, 111 and 112); correlation between QTc dispersion in MI and indirect measures of infarct size, such as ejection fraction (113); or the amount of viable myocardium in the infarct region (114). Similarly, significant correlation between QTc dispersion an left ventricular mass index in hypertensive patients with LVH was found in some studies (115, 116), but not in other (117).

Changes of QTc dispersion have been shown to follow the spontaneous or induced dynamicity of the pathological process in some cardiac diseases. For instance, QTc dispersion seems to undergo dynamic changes during the first day (118), as well as during the following days (119, 120), of acute MI. It increases significantly during ischemia induced by balloon inflation during angioplasty (121, 122 and 123), by exercise stress testing (124) or atrial pacing (125), or during reperfusion following angioplasty (126). It has also been shown to correlate with improvement of left ventricular contractility on the echocardiogram after infarction (127) and with the degree of improvement of left ventricular function after revascularization (128 and 129).

Treatment has been shown to decrease QTc dispersion, e.g., after successful reperfusion after thrombolysis (130 and 131), revascularization with angioplasty (132, 133 and 134) or coronary artery bypass grafting (129). Treatment of patients with heart failure with losartan (135), successful antihypertensive treatment of patients who had hypertension with LVH (136, 137, 138 and 139), or successful beta-blocker treatment of patients with long-QT syndrome (140) have also been shown to decrease QTc dispersion.

Prognostic value of QTc dispersion

Many studies have been aimed at investigating the value of QTc dispersion for the prediction of ventricular arrhythmias or other adverse events in various cardiac diseases. The results are again controversial.

Data from 23 studies on patients with and without serious ventricular arryhthmias in various cardiac diseases, most of them with ischemic heart disease. Altogether, 490 patients with and 1,341 patients without serious ventricular arrhythmias were included. Although most studies show significantly greater QTc dispersion in patients with arrhythmias, the values largely overlap.

Several studies, most of them retrospective, have found that patients with acute (141 and 142) or chronic MI (143, 144 and 145) with ventricular arrhythmias have significantly higher QTc dispersion than patients without arrhythmias. However, the first

prospectively analysed study in post-MI patient reported by Zabel et al. (146) showed that none of the 26 ventricular dispersion indices that were tested had any predictive value for an adverse outcome in 280 consecutive MI survivors followed up for 31 ± 10 months. Newer studies (147, 148) provided controversial findings.

Some studies showed that QTc dispersion could predict inducibility of ventricular arrythmias during electrophysiology study (149, 150 and 151), whereas other failed to observe this (152, 153 and 154).

Several studies (155, 156 and 157) showed significant correlation between QTc dispersion and outcome in patients with heart failure. Analysis (158) from the ELITE heart failure study, in which heart failure patients treated with the angiotensin-II antagonist losartan had reduction of sudden cardiac death compared with those treated with captopril (159), showed that captopril but not losartan increased QTc dispersion. However, the results of ELITE were not confirmed by the much larger double-blind. Randomized controlled ELITE-II trail (160), in which patients treated with losartan showed no significant differences in all-cause mortality, sudden death or resuscitated cardiac arrest compared with those treated with captopril.

Substudies of the DAMOND-CHF Study (161), the UK-HEART study (162) as well as other large prospective studies (163)

failed to show any power of QTc dispersion for predicting outcome in heart failure patients. Available studies also failed to show independent predictive value of QTc dispersion for sudden cardiac death and cardiac mortality in patients with LVH (164).

Several authors reported significantly higher QTc dispersion in HCM patients with ventricular arrhythmias compared with those without arrhythmias (165, 166 and 167). Larger studies, however, did not confirm these findings (168 and 169).

In long-QT syndrome, the diagnostic value of increased QTc dispersion seems undisputed. On the other hand, although Prior et al. (170) reported that patients not responding to beta-blockers had a significantly higher QTc dispersion than responders (137 ± 52 vs. 75 ± 38 ms, $p < 0.05$), no other presently available data suggest that QTc dispersion has any prognostic value in patient with long QT syndrome.

Generally, the positive results of small retrospective studies conducted in the years of initial enthusiasm were later confirmed only by some very large prospective studies. However, even in the large studies, patient groups with adverse outcomes often had QTc dispersion values well within both the measurement error and the range of values in healthy subjects reported in other studies. Thus, as phrased by Surawicz (171), the positive results can be interpreted as indicating an "indifferent" QTc dispersion. This does

not necessarily signify lack of clinical importance. In the majority of the cases, the abnormality was already visible from abnormal T wave morphology and increased QTc interval. At present, this does not necessitate a specific therapeutic action and, in practice, does not help in the risk stratification of individual patients.

Effect of drugs on QTc dispersion and the risk of torsades de pointes tachycardia

The limitations of both the presence and the degree of QTc interval prolongation for prediction of torsades de pointes are well known (172). Consequently, the potential role of QTc dispersion for the prediction of drug-induced torsade de pointes has been addressed in several studies.

Quinidine increase QTc dispersion (173 and 174) and, unlike the corrected QTc interval, increased QTc dispersion seems to have some predictive value for development of torsades de pointes during quinindine therapy (173 and 174). Sotalol has been shown to decrease (175) or not to change (176) QTc dispersion in patients with ischemic heart disease. However, Dancye et al. (177) observed increased QTc dispersion in 4 cases of torsades de pointes caused by low dose sotalol in patients with renal failure.

In clinical studies, amiodarone has been reported to decrease (176 and 178) or not to change (173, 179 and 180) QTc dispersion. It is known that amiodarone can be administered relatively safely in

patients who had experienced torsades de pointes during antiarrhythmic therapy with other drugs (181) and this effect is paralleled by a decrease of QTc dispersion (173). However, cases of an excessive increase of QTc dispersion and induction of torsades de pointes by amiodarone have also been reported (1820). On the other hand, it has been demonstrated that increase of QTc mean and QTc dispersion during chronic amiodarone treatment does not affect survival and is independent of the decrease in arrhythmia risk (183).

Propafenone (184), disopyramide (185) and almokalant (blocker of the rapid component of the delayed rectifier, I_{Kr}) (186) has been shown to increase QTc dispersion, whereas in one study dofetilide infusion did not produce increase of the dispersion of repolarization between two right ventricular endocardial sites (187). A decrease of QTc dispersion after treatment with aximilide (188) and magnesium has also been reported (189).

In addition to long QT syndrome (140) beta-blockers have been shown to decrease QTc dispersion in patients with syndrome X (190) and heart failure (191), but not in HCM (168).

Grossly abnormal values (e.g., $\geq$ 100 ms, unlikely to be due to measurement error) during treatment with drugs affecting repolarization signify "bad QTc dispersion" (171), which probably should prompt urgent assessment of the drug effect.

Indian perspective

With regard to the Indian perspective very few studies (200, 201) have been cited in literature. A study in India showed that means QTc dispersion in normal individual as 51.45 ± 5.56 msec (193). In a study by Parale et al. 100 patients with AMI were compared to controls. It was found that QTc dispersion was higher in patients with AMI compared to controls (109.11 ± 25.77 msec vs 51.45 ± 5.50 msec). QTc dispersion was found to be prolonged in patients who developed ventricular arrhythmias as compared to rest (148.57 ± 32.36 msec).

Materials and Methods

MATERIALS AND METHODS

Study Population and Design

The design was a cross sectional study comprising of 100 patients admitted with acute myocardial infarction to the Intensive Care Unit of Government Royapettah Hospital, Kilpauk Medical College during the period from January 2006 to July 2006. A control of 50 patients who were not diseased were screened and selected randomly from the outpatient department.

Inclusion Criteria

Patients with acute myocardial infarction with ST elevation getting admitted to Intensive Coronary Care Unit who were thrombolysed were included. The drug used for thrombolysis was streptokinase.

Exclusion Criteria

- Patients with Non ST elevation myocardial infarction were excluded .
- Patients with previous history of myocardial infarction.
- Patients with complete heart block.
- Patients with atrial fibrillation.
- Patients with history of intake of drugs prolonging QTc dispersion such as quinine, disopyramide, procainamide, tricyclic anti depressants and phenothiazines.

Selection of Controls

50 patients who had no history of any medical disease in the past were randomly selected from outpatient department after proper screening.

Data Collection and Assessment

Detailed questionnaire regarding history, examination findings were filled up for each patient. Assessment included baseline investigations, ECG and presence of any of the complications such as left ventricular failure, arrythmias and death.

History included enquiries regarding the time of onset of chest pain, dyspnoea, syncope, diabetes, hypertension, coronary heart disease and smoking .

Complete physical examination with specific note in arterial pulse, blood pressure, jugular venous pulse, auscultation of cardiovascular system and respiratory system were done at the time of admission, post thrombolysis and at the end of day one. ECGs were taken at the time of admission, post thrombolysis and after twenty four hours using HP page writer, besides this all patients had continuous ECG monitoring.

Heart rate, corrected QTc interval, shortest QTc, longest QTc and QTc dispersion were found out from twelve lead ECG at 25mmper second speed. Occurrence of arrhythmias, left

ventricular failure, death, post infarction angina were noted. The treatment regimens given, with special emphasis to usage of beta blockers and angiotensin converting enzyme inhibitors were also noted.

Corrected QTc was found out by application of modified Bazetts formula, QTc = QT in seconds/square root of RR interval in seconds. QTc is measured from the beginning of Q wave or R wave if Q is absent to the point at which descending limb of T joins the baseline. QTc was measured in all leads where T wave could be identified. QTc mean was calculated from QTc intervals of all the leads. QTc dispersion was calculated by the formula QTc maximum minus QTc minimum. In this way QTc dispersion was found out at the time of admission, post thrombolysis and twenty four hours later.

Statistical Methods

Comparisons were made between different groups such as diabetics and non diabetics, hypertensives and non hypertensives, smokers and non smokers, ischemic heart disease and no heart disease, AWMI and IWMI, patients in failure and not, dead and alive, those on beta blockers or ACE inhibitors.Mean QTc and QTc dispersion at admission, post thrombolysis and at 24 hours were calculated. Comparisons were made using student t test at three intervals separately. Later the probability of significance was

calculated based on the former. Values are expressed as mean ± standard deviation. Calculation was done using SPSS software with the help of our college statistician and researcher working for Indian Council For Medical Research. Using SPSS standard deviation, student t test and probability values were calculated.

Observations and Analsis

OBSERVATIONS AND ANALYSIS

TABLE -1

DISTRIBUTION ACCORDING TO AGE

Age	Number	Percentage
< 30	1	1
30-39	9	9
40-49	22	22
50-59	26	26
60-69	28	28
70-79	10	10
>80	4	4

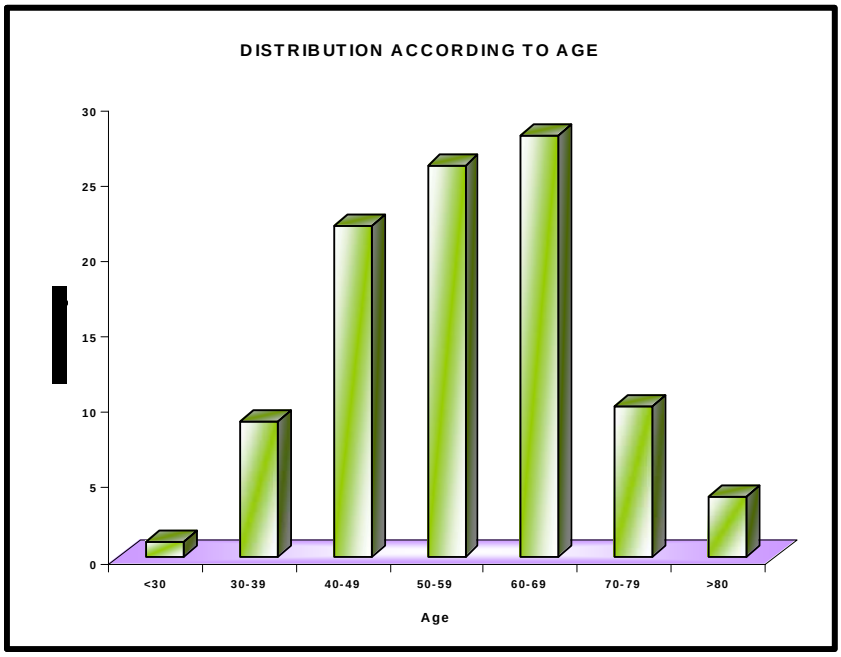
It is seen that most of the patients belonged to 50-69 yrs (54%). The mean was 55.34 yrs with a standard deviation of ± 12.73365.

TABLE- 2

DISTRIBUTION ACCORDING TO GENDER

Sex	Number	Percentage
Male	82	82
Female	18	18
Total	**100**	**100**

Most of the patients were males (82%). Only 18% were females.


DISTRIBUTION ACCORDING TO AGE
30
25
20
15
10
5
0
<30
30-39
40-49
50-59
60-69
70-79
>80
Age

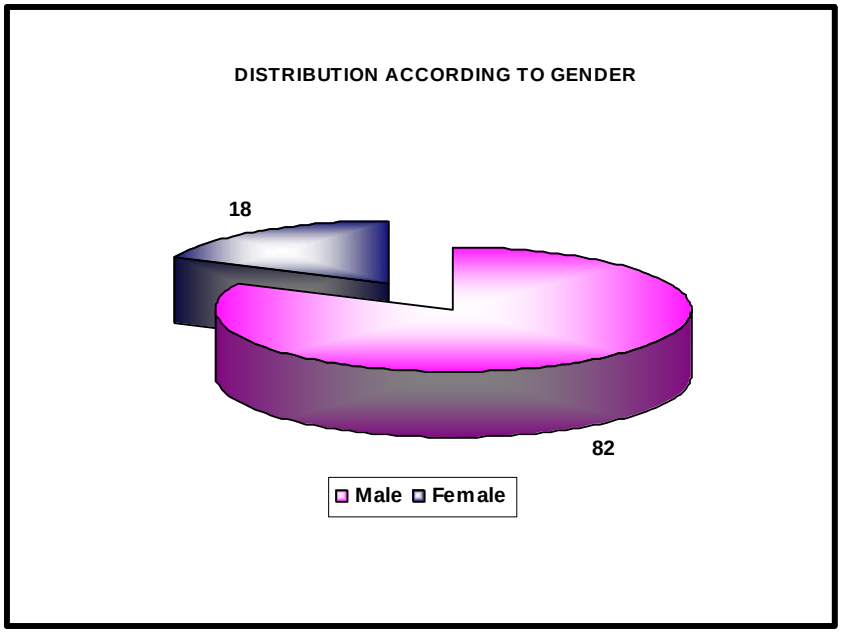
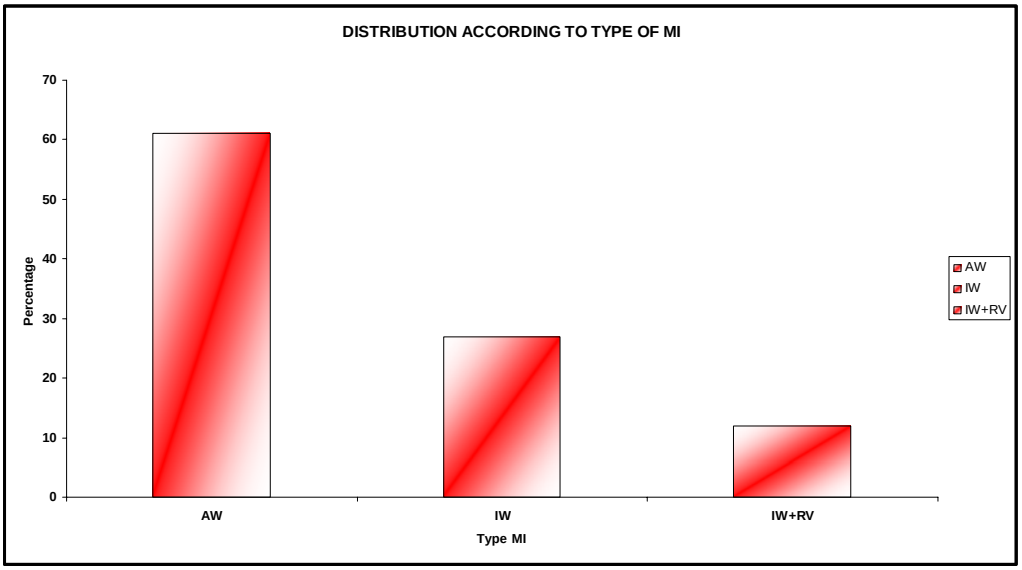

DISTRIBUTION ACCORDING TO GENDER
18
82
Male
Female

TABLE -3

DISTRIBUTION ACCORDING TO TYPE OF MI

Type MI	Number	Percentage
Anterior wall (AW)	61	61
Inferior wall (IW)	27	27
Inferior wall + right ventricular (IW+RV)	12	12
Total	100	100



Total 61 cases of anterior wall MI and 39 cases of inferior wall MI were taken. Of the 39 patients with IWMI, 12 had associated right ventricular MI.

TABLE – 4

DISTRIBUTION ACCORDING TO HISTORY OF TYPE 2 DIABETES MELLITUS

History of DM	Number	Percentage
Diabetics	23	23
Non diabetics	77	77
Total	**100**	**100**

Out of the 100 patients, 23 had type 2 diabetes mellitus.

TABLE -5

DISTRIBUTION ACCORDING TO HISTORY OF SYSTEMIC HYPERTENSION

Systemic hypertension (SHTN)	Number	Percentage
With history of SHTN	46	46
Without history of SHTN	54	54
Total	**100**	**100**

Of the 100 patients 46 were known hypertensives.

TABLE -6

HISTORY OF CORONARY ARTERY DISEASE (CAD)

History	Number	Percentage
CAD	28	28
No CAD	72	72
Total	**100**	**100**

28 patients had preexisting coronary artery disease, either unstable angina or chronic stable angina. Patients with pre existing myocardial infarction were excluded from the study.

TABLE-7

HISTORY OF SMOKING

History	Number	Percentage
Smoking	66	66
No smoking	34	34
Total	**100**	**100**

Majority of the patient were smokers 66%. None of the females were smokers, whereas 80.48% of male patients were smokers.

TABLE -8

BETA BLOCKERS

	Number	**Percentage**
Beta blockers	65	65
No Beta blockers	35	35
Total	**100**	**100**

Of the 100 patients, 65 received beta blockers meanwhile remaining 35 had some contraindication for Beta-blockers.

TABLE - 9

ACE INHIBITORS

	Number	**Percentage**
ACE inhibitors	79	79
No ACE inhibitors	21	21
Total	**100**	**100**

There were 21 patients who did not receive ACE inhibitors, remaining 79 patients received it.

TABLE -10

ARRHYTHMIAS

Arrhythmias	Number	Percentage
Ventricular arrhythmias	9	9
No Arrhythmias	91	91
Total	**100**	**100**

Of the 100 patients, 9 developed ventricular arrhythmias. Out of the 9, 7 developed ventricular tachycardia and two developed ventricular fibrillation.

TYPE OF MI IN PATIENTS WITH ARRHYTHMIAS

		No of Patients	Arrhythmias	Total
SEX	Male	77	5	82
	Females	14	4	18
AWMI	Non AWMI	36	3	39
	AWMI	55	6	61
IWMI	Non IWMI	55	6	61
	IWMI	36	3	39
RVMI	RVMI	12	0	12
	Non RVMI	79	9	88

Arrhythmias were more in males.

More among anterior wall MI patients.

Three patients with IWMI developed arrhythmias.

None among RVMI developed arrhythmias.

TABLE -11

CASE SUMMARIES

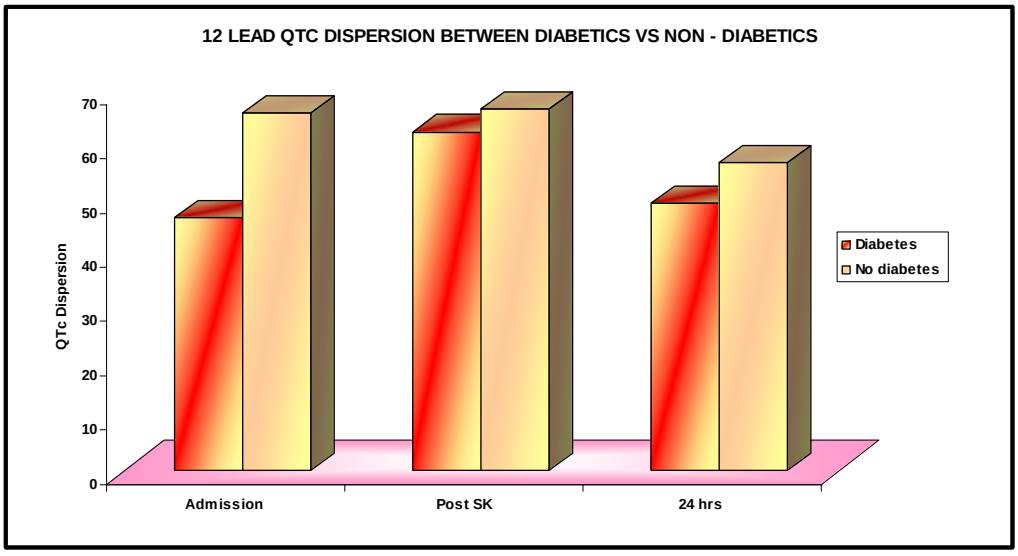
	Mean QTc dispersion	**SD**
Age	55.34	12.733
QTc Admission dispersion (12 lead)	61.59	42.578906
QTc post SK dispersion (12 lead)	65.81	35.59459
QTc at 24 hrs dispersion	55.17708	32.82521
QTc mean admission	422.79	40.20611

Mean age of the patients was 55 years. Mean QTc dispersion is given in the table. But standard deviation shows that the range was more at the time of admission and reduced on thrombolysis and at 24 hrs. This shows the protective role of thrombolysis on QTc dispersion.

TABLE -12

12 LEAD QTc DISPERSION IN DIABETICS AND NON DIABETICS

QTc dispersion	History of diabetes	Mean QTc	Standard deviation	P value
Mean	Diabetic	420.013	39.7351	0.207932
	No diabetes	432.0869	41.2640	
Admission	Diabetes	46.69565	33.58224	0.055465
	No diabetes	66.03890	44.13479	
Post SK	Diabetes	62.5456	25.25815	0.626421
	No diabetes	66.78378	38.22438	
24 hrs	Diabetes	49.40909	29.81476	0.350570
	No diabetes	56.89189	33.66742	



Comparison between diabetics and non diabetics was showing no significantly prolonged QTc dispersion in diabetics ($p>0.05$). Infact the study show slight reduction in QTc dispersion in diabetics.

TABLE – 13

QTc DISPERSION IN PATIENTS WITH AND WITHOUT SYSTEMIC HYPERTENSION

	History of hypertension	**Mean QTc / QTd**	**Standard deviation**	**P value**
QTc Mean	Hypertension	424.9348	45.84098	0.624907
	No hypertension	420.963	35.04227	
Admission	Hypertension	59.30435	43.96507	0.62272
	No hypertension	63.53704	41.87471	
Post SK	Hypertension	62.15909	33.70387	0.153319
	No hypertension	70.59615	36.76116	
24 hrs	Hypertension	55.79454	31.80652	0.885748
	No hypertension	54.73077	33.96602	

There was no statistically significant difference in QTc dispersion in patient with and without systemic hypertension. Though QTc mean was found be higher among hypertensives, QTc dispersion was lower in hypertensives than non hypertensives.

TABLE -14
TYPE OF MI AND QTc MEAN DISTRIBUTION

	Type	Mean QTc	Standard deviation	P value
AWMI	Yes (61)	426.4262	42.43994	0.260107
	No (39	417.1026	36.23737	
IWMI	Yes (27)	422.40741	34.16843	0.954201
	No (73)	4229315	42.43895	
RVMI	Yes (12)	405.1667	39.39966	0.105854
	No (88)	425.1932	39.39966	

Though QTc mean was found to be more in AWMI patients it was not statistically significant. No such relation could be seen with RVMI and IWMI. Though QTc dispersion was higher in IWMI compared to RVMI, it is was not statistically significant

TABLE – 15

QTc DISPERSION IN AWMI VS IWMI

	Type	Mean QTc dispersion	Standard deviation	P value
Admission	AWMI	63	44.6895	0.680934
	Non AWMI	59.38462	39.5159	
Post SK	AWMI	70.39655	36.27814	0.119563
	Non AWMI	58.81579	33.79817	
24 hrs	AWMI	53.7931	32.53541	0.612386
	Non AWMI	57.28947	33.58886	

Though QTc were higher in AWMI at admission & post SK but there was no statistical significance.

TABLE -16

QTc DISPERSION IN IWMI

	Type of MI	Mean QTc dispersion	Standard deviation	P value
Admission	IWMI	69.03704	36.63907	0.289758
	Non IWMI	58.8356	44.49126	
Post SK	IWMI	60.34615	32.07983	0.361875
	Non IWMI	67.84286	36.82494	
24 hrs	IWMI	55.84615	30.51126	0.903886
	Non IWMI	54.92857	33.51123	

Though QTc dispersion was more in IWMI at admission it reduced after thrombolysis and was not statistically significant.

TABLE -17

QTc DISPERSION IN RVMI

	Type	Mean QTc dispersion	Standard deviation	P value
Admission	RVMI (12)	37.66667	38.44555	0.037430
	Non RVMI(88)	64.85227	42.26532	
Post SK	RVMI (12)	55.5	38.5474	0.285669
	Non RVMI (88)	67.28571	35.15185	
24 hrs	RVMI (12)	60.41667	49.78649	0.557217
	Non RVMI (84)	54.42857	31.7533	

QTc dispersion was not increased in RVMI was statistically significant. This correlated with the least amount of arrhythmias in that group.

TABLE -18

QTc DISPERSION IN PATIENTS WITH AND WITHOUT LVF

	LVF	Mean QTc dispersion	Standard deviation	P value
Admission	LVF (+) (30)	73.666	47.5504	0.063014
	LVF (-) (70)	56.41429	39.550.19	
Post SK	LVF (+ (27)	68.66666	40.16983	0.625636
	LVF (-) (69)	64.69566	33.89053	
24 hrs	LVF (+) (27)	59.44928	39.24015	0.412560
	LVF (-) (69)	53.44928	30.09668	

QTc dispersion was significantly increased in patient with LVF and this was statistically significant especially at admission. Since four patients died soon after admission, post SK and 24 hrs study had only 96 patients.

TABLE - 19

QTc DISPERSION IN SMOKERS AND NON SMOKERS

	Type	Mean QTc dispersion	Standard deviation	P value
Admission	Smoker (66)	65.84849	33.9104	0.164603
	Non smoker (34)	53.32353	55.38062	
Post SK	Smoker (63)	67.90476	34.0084	0.429074
	Non Smoker (33)	61.81818	38.67044	
24 hrs	Smoker (63)	60.68254	34.27207	0.022365
	Non Smoker (33)	44.66667	27.97662	

QTc dispersion was significantly increased among smokers who had MI and this was statistically significant especially 24 hours after admission.

TABLE -20

QTc DISPERSION IN PATIENTS WITH AND WITHOUT CAD

	CAD	Mean QTc dispersion	Standard deviation	P value
Admission	CAD (+) (28)	61.60714	40.21824	0.998012
	CAD (-) (72)	61.58333	43.73471	
Post SK	CAD (+) (25)	53.25926	26.83367	0.844180
	CAD (-) (71)	55.92754	35.04235	
24 hrs	CAD (+) (25)	66.96296	33.6286	0.722308
	CAD (-) (71)	65.36232	36.56379	

QTc dispersion was slightly increased in those with CAD especially at admission and at 24 hrs but this was not statistically significant.

TABLE -21

QTc DISPERSION IN PATIENTS WITH BETA BLOCKERS AND WITHOUT BETA BLOCKERS

	Beta-Blockers	Mean QTc dispersion	Standard deviation	P value
Admission	Yes (65)	61.07692	37.00309	0.870534
	No (35)	62.54286	51.96059	
Post SK	Yes (64)	66.70313	32.79212	0.730794
	No (32)	64.03125	41.13901	
24 hrs	Yes (64)	54.45313	26.27506	0.761694
	No (32)	56.625	43.53993	

There appeared to be a reduction in QTc dispersion in those with Beta blockers especially at admission and at 24 hours, but it was not statistically significant.

TABLE -22

QTc DISPERSION IN PATIENTS ON ACE INHIBITORS AND NOT ON ACE INHIBITORS

	ACE Inhibitors	Mean	Standard deviation	P value
Admission	Yes (29)	58.96202	38.22049	0.233118
	No (71)	71.47619	56.096	
Post SK	Yes (77)	67.44156	35.34436	0.369447
	No (19)	59.21053	36.80969	
24 hrs	Yes (77)	55.71429	31.17	0.748716
	No (19)	53.3514	39.7316	

Though there was a decrease in QTc dispersion by ACE inhibitors at admission it was not sustained at post SK and at 24 hours. However none of these were statistically significant.

TABLE -23

QTc DISPERSION IN PATIENTS WITH AND WITHOUT ARRHYTHMIAS

	Arrhythmias	Mean QTc dispersion	Standard deviation	P value
Admission	Yes (9)	88.7778	2.1103	0.044049
	No (91)	58.9011	39.623	
Post SK	Yes (6)	69.5	25.493	0.7948
	No (90)	65.56667	36.261	
24 hrs	Yes (6)	37.3333	35.2344	0.170316
	No (90)	56.3666	32.5191	

QTc dispersion were increased in those with arrhythmias at admission which was statistically significant. However this was not sustained at 24 hrs and post SK. This is because of protective effect of streptokinase and treatment given.

TABLE - 24

MEAN QTc ANALYSIS AT ADMISSION

Variable		Mean QTc dispersion	S.D.	P value
Smoker	66 (Y)	419.5909	45.15954	0.269768
	34 (N)	429	27.79252	
CAD	28 (Y)	424.3214	37.66328	0.813626
	72 (N)	422.1945	41.39219	
Beta - blocker	65 (Y)	422.6769	37.57497	0.969659
	35 (N)	423	45.26848	
ACE inhibitors	79 (Y)	426.0253	40.05284	0.119105
	21 (N)	410.219	39.35032	
Diabetes	23 (Y)	420.013	39.7351	0.207932
	77 (N)	432.0869	41.2640	
Hypertension	46 (Y)	424.9348	45.84098	0.642903
	54 (N)	420.963	35.04227	
Death	9 (Y)	452. 2222	40.03996	0.020549
	91 (N)	419.8791	39.24902	
LVF	30 (Y)	435.1667	35.48393	0.043289
	70 (N)	417.4857	41.17081	

There appears to be no statistically significant effects on QTc mean by diabetes, Hypertension, Smoking, CAD, Beta-blockers and ACE inhibitors. However there was statistically significant correlation between death, LVF and QTc mean.

TABLE – 25

QTc DISPERSION IN PATIENTS WHO DIED

	Alive VS Dead	**Mean QTc dispersion**	**Standard deviation**	**P value**
Admission	Dead (9)	85.6666	66.59955	0.075212
	Alive (91)	59.2879	39.19453	
Post SK	Dead (9)	55.2	33.80282	0.496396
	Alive (91)	66.39561	35.80282	
24 hrs	Dead (9)	49.6	23.6072	0.698552
	Alive (91)	55.48352	33.32812	

QTc dispersion was significantly increased in those who died especially soon after admission. However this effect was not sustained and there was no statistical significance to any of the remaining data analysed. The protective role of thrombolysis could been seen by the reduction of QTc dispersion at post thrombolysis and at 24 hrs.

ANALYSIS OF CONTROLS

Distribution of Age

Sex	Mean	Standard Deviation
Males	49.9166	15.12536
Females	52.76923	13.61266

Distribution of Mean

Sex	Mean QTc	Standard Deviation	P Value
Males	380.1667	78.47828	0.06743
Females	414.362	43.85516	

Distribution of QTc dispersion

Sex	Mean QTc dispersion	Standard Deviation	P Value
Males	47.58333	18378	0.25798
Females	53.5	17.52	

Discussion

DISCUSSION

In the present study, 100 patients with acute myocardial infarction were considered for QTc dispersion evaluation . This included 61 patients with AWMI, 27 patients with IWMI and 12 patients with RVMI. A control group of 50 asymptomatic patients were also included.

Of the 100 patients, most of patients ie ,54 belonged to 50-69 years age group (26 patients in 50 – 59 yrs and 28 patients in 60-69 yrs). Mean age was 55.34. In other trials such as by Zabel et al (198) it was 57 yrs. Average age in Indian study by Yadav et al (200) was 51.2 yrs and Reddy et al (201) was 50.37 yrs. One patient was less than 30 yrs and was a heavy smoker. However Macfarlane et al (11) found no significant age difference in QTc dispersion.

Majority of the studies in acute myocardial infarction showed male preponderance. In our study also males dominated (82%). Out of 18 females only two (12%) were less than 50 yrs, remaining 16 (88%) were more than 50 yrs. This reiterates the protective role of Oestrogen on coronary vessels in premenopausal age. This ratio was comparable in other trials also (Zabel et al (198) 82% vs 18% and Yadav et al (200) 84% vs 16% and Reddy et al (201) 85% vs 15%. The ratio was little more in Japanese study of Endoh Y et al (197) 75% vs 25%).

31% of the IWMI were having RVMI. This emphasizes the need for taking right ventricular leads routinely in all patients apart from standard 12 lead ECG presenting with AMI. According to Reddy et al he had 54% patients with RVMI and IWMI combined.

The study also raises concern regarding increasing burden of diabetes in Indian population (23%). This may be due to Berkisonian bias. This is more than the prevalence in other Indian and Western studies (12% Reddy et al (201), Yadav et al (200), 13.7 Hopkin e al (202)). A comparison between mean QTc in Diabetics (420.013 ± 39.73) and non diabetics (432.08 ± 41.23) ($p = 0.2079$) showed no statistical significance. There was no significant relation of QTc dispersion between diabetics and non diabetics.

66% of patient were smokers. This is more than other studies such as Reddy et al (201) (52%), Yadav et al (200) (58%) and Hopkins et al (202) (55%). This may be due to other enviromental factors like lifestyle changes and sedentary habits. Hence this is a potential reversible factor and there is plenty of scope for health education as preventive measure.

Systemic hypertension was present in 46% of the study subjects. This is accordance with Hopkins et al (202) (46%), however much more than the Indian studies by Reddy et al (201) (24%) and Yadav et al (200) (22%). This high incidence may be due

to life style changes like smoking and once again there is scope for health education and potential reversibility.

Comparison between AWMI and IWMI showed that QTc dispersion is increased in both [63 m sec and 69 m sec (admission) : 70m sec and 60 m sec (streptokinase) : 53 m sec and 55 m sec (at 24hrs)] and was not statistically significant ($p > 0.05$). This is not consistent with Morena et al who showed significant increase in QTc dispersion after AWMI vs IWMI. However there was a statistically significant relation of QTc dispersion in those with RVMI ($p = 0.0374$). This observation perhaps has implication to keep those patients with RVMI under strict monitoring.

Significant reduction in QTc dispersion after thrombolysis (69 m sec vs 60 m sec) were seen in those with IWMI which was in accordance with (193) Parale et al (109.11 vs 87.59) and (203) Karagonius et al (75 m sec vs 53m sec). This emphasize the beneficial effect of thrombolysis. However in this study no significant reduction was observed in those with AWMI and RVMI.

QTc dispersion after AMI (AWMI 63 m sec, IWMI 69 m sec) were in accordance with western studies (Karagonius et al 74 m sec ± 38, (199) Hugham P.D. et al – 75 m sec). This observation suggest that genetic and ethnic factors may play a role in QTc dispersion . Further studies are warranted in this respect.

QTc dispersion were increased in those with left ventricular dysfunction compared with those not in failure (admission 73 vs 56 ; post SK 68 vs 64 ; at 24 hrs 59 vs 53 m sec) but none of these were statistically significant. This is in accordance to Karagonius et al (75 m sec vs 53m sec). Further large scale studies are warranted regarding this aspect (86, 87, 88, 89).

Patients with CAD showed a slight increase in QTc dispersion , however it was not statistically significant. This was in accordance with Ashihaga et al (84) and Sporton et al (85).

Patients treated with beta blockers showed a reduction in QTc dispersion especially at admission (61 vs 62 m sec) , at 24 hrs (54vs 56m sec) and it was not statistically significant. However this is in accordance with Leonardo et al (190) who found out that beta blockers will decrease QTc dispersion . The smaller reduction in our study may be due to a smaller sample size. However ACE inhibitors showed a reduction in QTc dispersion at admission which was not sustained during post SK and at 24 hrs. None of these were statistically significant.

Most importantly QTc dispersion were significantly increased in those with ventricular arrhythmias compared to non arrhythmic group (88 vs 58 m sec at admission ; 69 vs 65 m sec post SK). This was statistically significant ($p = 0.04$). The comparative reduction in QTc dispersion in post SK and 24 hours may be due to a

conglomerulation of protective effects by thrombolysis and other drugs such as ACE inhibitors . This is in accordance with studies of (196) Zaputovic et al (77 ± 23 vs 53 ± 27m $p<0.01$). In study by (199) Hugham PD et al it was 105m sec vs 75 m sec at admission. Study by Parale et al showed significant difference in QTc dispersion (148 ± 32.36 vs 105.85 ± 20.24 m sec). This reiterates the role of QTc dispersion in predicting arrhythmias. This can be useful for risk stratification.

QTc dispersion was significantly increased in patients who died especially at the time of admission (85 vs 59 m sec, $p = 0.075$) but was not statistically significant.

Analyzing the QTc dispersion in normal control population showed 47.5833 ± 18.73 m sec in males and 53.5 ± 17.52 m sec in females which is in accordance with Kairtzner et al (70) and Staller et al (71) who reported normal values are between 30 and 70 m sec. The mean age of control group was 49.9 ± 15.1 years in males and 52.7 ± 13.6 years in females.

Analyzing the QTc mean showed no statistical correlation in patients with history of smoking, CAD, those being treated with beta blockers and ACE inhibitors. However mean QTc were prolonged in those who had left ventricular failure (435 ± 35 vs 417 ± 41 m sec) and those who died (452 ±40 vs 419 ± 39 m sec), both were statistically significant ($P<0.05$).

Conclusion

CONCLUSION

- QTc dispersion was more and statistically significant in those with left ventricular failure at admission.
- QTc dispersion was more and statistically significant in smokers after the first day of infarct.
- QTc dispersion was more and statistically significant in those with ventricular arrhythmia at the time of admission.
- QTc dispersion was more but not statistically significant in those who died.
- There was positive correlation between usage of ACE inhibitors and QTc dispersion reduction at the time of admission which was not to be seen in post SK and at 24 hrs.
- There appeared to be a reduction in QTc dispersion in those with Beta-blockers especially at admission and at 24 hours, but it was not statistically significant.
- QTc dispersion was slightly increased in those with CAD especially at admission and at 24 hrs but not statistically significant.
- Comparison between diabetics and non diabetics showed no significant QTc dispersion in diabetics ($P>0.05$). Infact the study show slight reduction in QTc dispersion in diabetics.
- There was no statistically significant difference in QTc dispersion in patients with and without systemic hypertension. Though QTc mean was found be higher among

hypertensives , QTc dispersion was lower in hypertensives than non hypertensives.

- Though QTc mean was found to be more in AWMI patients it was not statistically significant. No such relation could be seen with RVMI and IWMI. Though QTc dispersion was higher in IWMI compared to RVMI, it is was not statistically significant
- The normal QTc dispersion among healthy Indian individuals corresponds to those of western data.
- Though QTc dispersion was higher in AWMI at admission & post SK there was no statistical significance.
- QTc dispersion was increased in those with arrhythmias at admission which was statistically significant. However this was not sustained at 24 hrs and post SK. This could be because of protective effect of streptokinase and treatment given.
- QTc dispersion were significant increased in those dead especially at the time of admission. However this effect was not sustained and there was no statistical significance to any other data analysed. The protective role of thrombolysis could be seen by the reduction of QTc dispersion at post thrombolysis and at 24 hrs.
- There was statistically significant correlation between left ventricular failure and QTc mean.

- The role of QTc dispersion in the present scenario should be questioned as most of the parameters correlated negatively except for LVF and arrhythmia (3).

Summary

SUMMARY

QTc dispersion was more and statistically significant in those with left ventricular failure at admission. QTc dispersion was more and statistically significant in smokers after the first day of infarct. QTc dispersion was more and statistically significant in those with ventricular arrhythmia at the time of admission. QTc dispersion was more but not statistically significant in those who died. There was positive correlation with usage of ACE inhibitors and QTc dispersion reduction at the time of admission which was not to be seen in post SK and at 24 hrs. There was no significant correlation between beta blockers and QTc dispersion. There was no significant correlation between CAD patients and QTc dispersion. There was no significant correlation between diabetes and QTc dispersion. There was no significant correlation between hypertension and QTc dispersion. There was no significant correlation between the type of infract and QTc dispersion. The normal QTc dispersion among normal Indian individuals corresponds to those of western data. There was no statistically significant difference in QTc mean and various types of myocardial infarction. There was a statistically significant positive correlation between incidence of arrhythmia and QTc mean. There was statistically significant positive correlation between death and QTc mean. There was statistically significant correlation between left ventricular failure and QTc mean.

Contrary to the initial expectations, QTc dispersion did not evolve into a useful clinical tool. Although this simple ECG parameter is probably not (only) a result of measurement error, it does not reflect directly and in quantifiable way the dispersion and the heterogeneity of the ventricular recovery times. The standard 12-lead ECG contains information about regional electrical phenomena, but this information cannot be extracted by such a simple technique as QTc dispersion assessment.

In addition, not only the magnitude of dispersion of recovery times, but the distance over which they are dispersed is important for arrhythmogenesis. In a similar way as we distinguish, though arbitrarily, "micro reentry" from "macro reentry," it seems logical to distinguish dispersion of recovery times of adjacent areas (global dispersion) and possible, from dispersion between both ventricles (interventricular dispersion). Such a scale is clearly beyond the resolution of the standard surface ECG. Local dispersion of recovery times created by MI is no more visible on the standard surface ECG than the delayed conduction caused by the same infarct.

The very idea of detecting and quantifying only the dispersion of the end of repolarization, i.e., the dispersion of the complete recovery times, also seems questionable. Action potentials of different duration usually have very different shape, particularly during phase 3. Such a "phase 3 dispersion," i.e., the dispersion of

the partial recovery times, has direct relation to arrhythmogenesis. Although it is reflected in the shape of the T wave, it does not contribute to the dispersion of the ends of the MAPs, let alone the dispersion of the QTc intervals.

In a recently published experimental study Shimizu et al. (192) showed that the T wave alternans induced by rapid pacing were a result of alterations in the APD of the M-cells, leading to exaggeration of transmural dispersion of repolarization during alternate beats and thus to the potential for developmental of torsades de pointes. The result of the study clearly emphasized that spatial dispersion of the recovery times cannot be estimated without the analysis of the morphology of the T wave, as well as without taking into account its dynamicity.

Similarly in this study too, the efficacy of QTc dispersion as prognostic indicator does not faithfully impress on itself. This is because there was considerable overlap between QTc dispersion in controls and MI patients. Moreover QTc dispersion was found to be significantly increased only in left ventricular failure, arrhythmias ,patients who died whereas in other comparisons made there was no significant positive correlation.

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ABBREVIATIONS

β (-)	Beta blocker
ACE (-)	Angiotensin converting enzyme inhabitor
AMI	Acute myocardial infarction
APD	Action potential duration
AWMI	Anterior wall myocardial infarction
CAD	Coronary artery diseases
CI	Confidence interval
DM	Diabetes mellitus
ECG	Electrocardiogram
HCM	Hypertrophic cardiomyopathy
HP	Hewlett packard
IWMI	Inferior wall myocardial infarction
LVF	Left ventricular failure
MAP	Monophasic action potential
MI	Myocardial infarction
QTc	QT interval corrected
QTd	Corrected QT dispersion
RVMI	Right ventricular myocardial infarction
SHTN	Systemic hypertension
SK	streptokinase

QTc DISPERSION IN ACUTE MYOCARDIAL INFARCTION

PROFORMA

Name : Age :

Sex : Male / Female Occupation :

Date of Admission : IP No.:

Date of discharge : Date of MI and index pain :

History	Yes	No	Duration
Chest pain			
Dyspnoea			
Syncope			
Resuscitated Cardiac arrest			
h/o diabetes mellitus			
h/o hypertension			
h/o coronary artery disease			
h/o smoking			

Examination	Pulse	BP	JVP	CVS	Chest
At admission					
24 hrs					
48 hrs					

Treatment given	Yes	No
Beta blockers		
Ace inhibitors		
Aspirin		
Clopidogrel		
Nitrates		

	Admission	Post SK	24 hrs after
ECG			
Mean QTc			
Shortest QTc			
Longest QTc			
QTc dispersion in 12 led ECG			

	Yes	No
Arrhythmias		
Post infarction angina		
Reinfarction		
Clinically detected left Ventricular failure		
Death		